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Pharmacokinetic and Pharmacodynamic Reactions to Clopidogrel: Confirmations and Points of View

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INTRODUCTION

Overall, clopidogrel reduced the rate of recurrent atherothrombotic events in patients with severe coronary artery disease (ACS) and in patients undergoing percutaneous coronary intervention (PCI). However, relapses persisted, possibly due in part to inadequate platelet blockade by standard treatment with clopidogrel. Genetic polymorphisms associated with clopidogrel ingestion, ingestion, and the P2Y12 receptor may reduce its antiplatelet activity. Late evidence suggests that epigenetic regulation may also affect response to clopidogrel. In addition, non-genetic factors such as socioeconomic factors, infectious factors, and drug combinations may influence the antiplatelet effect of clopidogrel. There is particular evidence that factors that add to the diversity of clopidogrel response will further develop platelet obstruction and reduce the risk of cardiovascular events. Dual antiplatelet therapy with headache medicine and P2Y12 inhibitors is important for patients with severe coronary artery disease (ACS) and percutaneous coronary mediated (PCI) to prevent the chance of thrombosis in future.

DESCRIPTION

Clopidogrel, an orally irreversible antagonist of the P2Y12 receptor, is commonly used in clinical practice unlike other P2Y12 antagonists, eg: Ticagrelor or prasugrel. Following oral administration, approximately 85% of the clopidogrel prodrug is hydrolyzed by esterases to the latent structure, leaving only 15% of clopidogrel metabolized to the active metabolite by cytochrome P450 (CYP450) liver, of which CYP2C19 is important. Compounds. However, large studies have shown large individual variability in the antiplatelet effects of clopidogrel. Impaired platelet reactivity to clopidogrel may lead to an increased risk of cardiovascular events. Various studies have shown a relationship between the CYP2C19 polymorphism and the antiplatelet effect of clopidogrel. Furthermore, various factors including epigenetics, socioeconomics, concurrent infections and drug cooperation may contribute to this unfortunate response. Our study attempts to identify multiple factors influencing pharmacodynamics and pharmacokinetics that may explain the underlying components of clopidogrel response variability. Paraoxonase-1 (PON1) is an esterase that is regulated in the liver and binds to HDL (high-density lipoprotein) cholesterol. A previous report showed that PON1 is an essential protein for the biotransformation of clopidogrel to its active metabolite by hydrolysis of the c-thiobutyrolactone ring of 2-oxo-clopidogrel. The PON1 variant Q192R (rs662) was originally thought to have an even more effective effect on clopidogrel. However, the accompanying reviews did not repeat the results published that the inherited Q192R variant was not associated with pharmacological or clinical response to clopidogrel, and the results of a meta-survey including 13 reviews also showed no truly great relationship between 192Q variant and cardiovascular events treated with clopidogrel In addition, the work of Dansette showed that second-step enzymatic transformation relies mainly on the P450 pathway from 2-oxo-clopidogrel to 4b cis, but also relies on PON1 to the secondary 4b “endo” metabolite, which is still antiplatelet metabolites [1-4].

CONCLUSION

These results suggest that the role of PON1 in clopidogrel obstruction may be insignificant. However, pharmacokinetic genetic studies have found several SNPs involved in clopidogrel responses, the impact of most polymorphisms on a wide variety of platelet activities has yet to be fully confirmed with the exception of CYP2C19 LOF. Late assessments demonstrated that epigenetic alterations in traits related to drug attitudes or effects can also influence drug response.

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Epigenetic alterations can affect match quality and chromosomal structure without altering the nucleotide pool, and are also influenced by physiological and obsessive circumstances as well as natural variables. Interest in epigenetic studies of the clopidogrel response has also increased in recent times. Much of this clopidogrel review focuses on microRNA and DNA methylation.

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CONFLICT OF INTEREST

Authors declare no conflict of interest.

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